REMARKS

The Office Action

Claims 37, 38, 40-42, 45, 46, 48-50, 53, 54, 56-58, 61, 63-68, and 70-76 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 37-76 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 37, 38, 40-42, 45, 46, 48-50, 53, 54, 56-58, 61, 63-68, and 70-76 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Zhou et al (1997) *EMBO J.* 16: 3207-3218. This is a new rejection, as noted below, and Applicants have asked that the finality of this Office action be withdrawn, as noted below.

Claims 37-76 are rejected under the judicially-created doctrine of obviousness-type double patenting. These are provisional rejections.

Amendments

These amendments were made in response to the Examiner's rejections, and were not made previously for that reason.

Claims 38, 43, 46, 51, 54, 59, 66, and 73 have been cancelled.

The presently amended claims are directed to:

transgenic plants having enhanced tolerance to fungal disease, comprising a recombinant polynucleotide encoding SEQ ID NO: 18 (G28 polypeptide);

methods for enhancing the disease tolerance or resistance of a plant comprising transforming a plant with a recombinant polynucleotide encoding G28, SEQ ID NO: 18;

methods for altering the expression levels of at least one gene in a plant by transforming the plant with a recombinant polynucleotide encoding G28, SEQ ID NO: 18, and the transgenic plant has enhanced tolerance to fungal disease;

transgenic plants having enhanced tolerance to fungal disease, comprising a recombinant polynucleotide comprising a nucleotide sequence encoding a transcription factor having a conserved domain of a plant AP2 transcription factor, where the nucleotide sequence encoding said transcription

factor hybridizes under high stringency conditions (0.2 x SSC and 0.1% SDS at 65° C) to a polynucleotide sequence encoding an amino acid sequence of residues 145-213 of G28, SEQ ID NO: 18;

methods for enhancing the disease tolerance or resistance in a plant comprising transforming the plant with a recombinant polynucleotide comprising a nucleotide sequence encoding a transcription factor having a conserved domain of a plant AP2 transcription factor, where the nucleotide sequence that encodes the transcription factor hybridizes under high stringency conditions (0.2 x SSC and 0.1% SDS at 65° C) to a polynucleotide sequence encoding a conserved domain comprising an amino acid sequence of residues 145-213 of G28, SEQ ID NO: 18; and

transgenic plants with enhanced tolerance to fungal disease, comprising a recombinant polynucleotide encoding a transcription factor of G28, SEQ ID NO: 18, or the same sequence with one or more conservative substitutions, deletions, or insertions.

Support for amendments to Claims 37, 45, 53, 61, 68 and 75 may be found, for example, in the specification on page 5, line 10 (in which the SEQ ID NO: of G28 is identified), on page 7, lines 22-35 (fungal disease tolerance), and in the claims as originally filed.

The amendments to Claims 44, 52, 60, 67, and 74 are made because these claims previously depended from claims that have now been cancelled. Support for these amendments is provided by, for example, the claims as filed (see, for example, Claims 1 and 5, which are directed to altered disease tolerance or resistance, or Claim 20, directed to a transgenic plant having an improved disease tolerance or resistance), and by Example VII, in which transgenic plants that are pathogen resistant or tolerant showed a delay in *Fusarium or Erysiphe*-caused disease compared to wild-type control plants, and by the Heard declaration, previously submitted, which supports the instant claims by presenting data showing how plants transformed with G28 are more tolerant to *Fusarium, Erysiphe, Sclerotinia* or *Botrytis*.

Applicants believe that no new matter enters by the new claims, and request entry of the amendments and reconsideration of the application. Applicants specifically reserve the right to seek patents for all the sequences and subject matter disclosed in the application and original claims that is not currently being examined. The amendments are not made for reasons of patentability.

Response to Rejections

Section (8) of the rejection: 35 U.S.C. § 112, first paragraph

Claims 37, 38, 40-42, 45, 46, 48-50, 53, 54, 56-58, 61, 63-68, and 70-76 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants believe that this part of the rejection has been avoided by the amendment of the claims.

In paper 25, page 3, fourth paragraph, the Examiner states

> **"Applicant does not describe a transgenic plant comprising a recombinant polynucleotide encoding a transcription factor comprising a conserved domain of a plant AP2 transcription factor wherein said transcription factor has at least 42% sequence identity with SEQ ID NO: 18, wherein said transcription factor comprises an amino acid sequence of residues 145-213 of SEQ ID NO: 18 having one or more conservative substitutions, deletions or insertions, and said polynucleotide hybridizes under unspecified stringency conditions to a polynucleotide sequence encoding an amino acid sequence of residues 145-213 of SEQ ID NO: 18, and methods of making same."**

As the Examiner has noted on page 5, second paragraph of paper 25:

> **"those claims directed to transgenic plants comprising a recombinant protein having the amino acid sequence of SEQ ID NO: 18 are not included in the instant rejection."**

In the specification as filed, Applicants identified the function of the G28 polypeptide, SEQ ID NO: 18, which was later confirmed, as noted in the Heard declaration (previously filed, and as noted by the Examiner). Amended claims 37, 39-42, 44-45, 47-50, 52-53, 55-58, and 60 are directed to transgenic plants comprising a recombinant protein having the amino acid sequence of SEQ ID NO: 18. These claims are no longer directed of 42% sequence identity with SEQ ID NO: 18, and thus avoid this part of the rejection.

As to the breadth of the remaining claims, which are directed to nucleotide sequences that hybridize under high stringency conditions to a polynucleotide sequence encoding a conserved domain comprising an amino acid sequence of residues 145-213 of SEQ ID NO: 18, the claims are believed by Applicants to be adequately described for the following reasons.

Contrary to the "unspecified stringency conditions" stated by the Examiner, independent claims 61 and 68 were quite specific by being directed to conditions according to the phrase: "said high stringency conditions comprise 0.2 x SSC and 0.1% SDS at 65° C".

In fact, the specific claims language is better defined and refers to more stringent conditions than that used in the USPTO's "Synopsis of Application of Written Description Guidelines", which defines stringent conditions that meet the written description requirement as "6x SSC and 65° C" (page 35-36, copy attached). More to the point, the hybridization conditions are not found in the claim of Example 9 in the "Guidelines", but are instead identified in the specification.

As these Guidelines note: a "person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent conditions set forth in these claims yield structurally similar DNAs. Thus, ***a representative number of species is disclosed, since highly stringent conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention***" (p. 36-37, attached; ***emphasis*** added).

Thus, the USPTO has determined that a less stringent description of hybridization to a specific polynucleotide sequence under conditions less stringent than presently claimed is sufficient to yield structurally similar DNAs, and meet the written description requirement.

Regarding the amino acid sequence of residues 145-213 of SEQ ID NO: 18, the specification notes that amino acid residues 145-213 correspond to the conserved domain of SEQ ID NO: 18 (Table 1a). The Examiner has stated that "one of skill in the art would...inherently recognize a polypeptide sequence as having an AP2-like domain and would not speculate that said polypeptide sequence is a transcription factor" (paper 25, page 5, paragraph 3 to page 6, paragraph 1). As one skilled in the art would be aware, functional domains are conserved across evolution, and "structure and molecular function [are] largely conserved within domain families" (from a seminar given by Stephen H. Bryant, NCBI, at MIT, March 2003, abstract attached). In the Zhou et al. reference cited by the Examiner, the correlation between Pti4, which has considerable similarity to the conserved domain of G28, was used to search the GenBank database to find other proteins that function in a similar manner to Pti4, thus underscoring the recognition that these similar proteins share similar functions. Also according to Zhou, Pti4 is "similar to the tobacco ethylene-responsive element-binding proteins" which also function to defend plants from pathogens by inducing the expression of "pathogenesis-related" (PR) genes.

Regarding transcription factors encompassed by the scope of the claims beyond SEQ ID NO: 18, the Examiner has noted that it may be difficult to correlate precise function with the structure of an encoded AP2 transcription factor, and cited the Riechmann et al. (1998) reference. However, Riechmann reference makes note of this difficulty by stating: "the EREBP subfamily members so far characterized appear to be involved in responses to biotic and environmental stress, although their precise functions are largely unknown ***because no mutants for the corresponding genes have yet been isolated***" (***emphasis*** added). While this citation supports the function of response to abiotic stress by members of this gene family, it has no bearing on the written description of the invention found in the present specification. The fact that Riechmann and Meyerowitz had not, as of June 1998, identified mutants to determine the function of G28 and related proteins did not preclude or prevent others, including Applicants, from conducting and filing these studies at a later date (March, 1999), with disclosure of transgenic plants transformed with G28 and other transcription factors. It is unfortunate that Riechmann and Meyerowitz did not have these data at hand for their publication, but fortunate that the present specification is able to provide these data and associate function with G28 and structurally related genes. To suggest otherwise is to suggest that, once something has been reported as unknown, all subsequent studies and publications are doomed to be unrevealing rather than being elucidating.

The Examiner has also cited University of California v. Eli Lilly and Co., 43 USPQ2d 1398 (Fed. Cir. 1997), and MPEP §2163. However, in Enzo, 296 F.3d at 1328, (Fed. Cir. April 1, 2002) and in Moba, B.V., Staalkat, B.V., and FPS Food Processing Systems, Inc., v. Diamond Automation 01-1063, -1083 (Fed. Cir. April 1, 2003), the court noted:

> **"Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, [HN15] the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure."**

For the reasons stated above, Applicants believe that, in fact, the written description requirement has been satisfied for the instant claims because in the knowledge of the art, the disclosed function is sufficiently correlated to a particular, known structure:

a function was associated with the sequence of G28;

the G28 conserved domain subsequence was disclosed in Table 1a;

a representative number of species was disclosed, since highly stringent conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention; and

the knowledge in the art of conservative substitutions, deletions and additions, the description of such alterations in the specification, and the limitation that such alterations must be similarly functional to G28, would provide sufficient written description to one skilled in the art that Applicants were in possession of the claimed invention at the time of filing.

Accordingly, Applicants request that this portion of the rejection be withdrawn.

Section (9) of the rejection: 35 U.S.C. § 112, first paragraph

Claims 37-76 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims were rejected because the Examiner is concerned that

> **"[t]he instant specification provides no guidance to one of skill in the art as to what function a polypeptide having the amino acid sequence shown in SEQ ID NO: 18 has, or how to use a transgenic plant comprising a recombinant polynucleotide encoding said polypeptide as claimed."**

Contrary to this statement, the instant specification provides extensive guidance as to the nature and function (pathogen resistance or tolerance) of a polypeptide having the amino acid sequence shown in G28 (SEQ ID NO: 18), and also provides considerable guidance with respect to how to make and use (see, for example, Example VII, page 24) a transgenic plant comprising a recombinant polynucleotide encoding said polypeptide as claimed. Also see, for example:

page 1, lines 28-29 ("[t]he present invention provides transcription factors for use in modifying a plant's disease tolerance or resistance");

page 1, line 37-page 2, line 2 ("the presence of the recombinant polynucleotide alters the disease tolerance or resistance of the transgenic plant...");

page 4, lines 4-10 ("[e]xemplary polynucleotides or polypeptides comprise a sequence provided in the Sequence Listing as ... SEQ ID No.17 (G28), SEQ ID No.18 (G28 protein)";

page 7, lines 22-27 ("[w]e have discovered particular plant transcription factors (TFs) that are induced when plants are exposed to either biotropic or necrotropic pathogens.. These transgenic plants

may be more resistant to biotrophic or necrotrophic pathogens such as a fungus, ... in particular, pathogens such as *Fusarium oxysporum*, *Erysyphe* (sic) *orontii* and other powdery mildews, *Sclerotinia spp.*, ... *Botrytis spp*");

page 7, line 36 ("[t]hese transcription factors can be used to modulate a plant's response to disease");

page 17, lines 10-15 ("[t]he plants may have commercial utility for increasing tolerance or resistance to pathogens and pests. These transgenic plants may be more resistant to biotrophic or necrotrophic pathogens or belonging to the following groups such as a fungus ... or the like and associated diseases. In particular, pathogens such as *Fusarium oxysporum*, *Erysyphe orontii* and other powdery mildews, *Sclerotinia spp* ... *Botrytis spp* ... [t]he diseases include fungal diseases such as rusts, smuts, wilts, yellows, root rot, leaf drop, ergot, leaf blight of potato, brown spot of rice, leaf blight, late blight, powdery mildew, downy mildew, and the like");

Claim 1 ("[a] transgenic plant comprising a recombinant polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising at least 6 consecutive amino acids of a sequence selected from the group consisting of SEQ ID Nos. 2N, where N=1-56, wherein the recombinant polynucleotide alters the plant's disease tolerance or resistance when compared with the same trait of another plant lacking the recombinant polynucleotide"); and

Claim 5 ("[a] A method for altering the disease tolerance or resistance of a plant, said method comprising (a) transforming a plant with a recombinant polynucleotide comprising a nucleotide sequence encoding a polypeptide comprising at least 6 consecutive amino acids of a sequence selected from the group consisting of SEQ ID Nos. 2N, where N=1-56, (b) selecting said transformed plants; and (c) identifying a transformed plant having an altered disease tolerance or resistance").

Thus, Applicants identified the G28 (SEQ ID NO: 18) polypeptide sequence, showed how to make transgenic plants in great detail, and deduced that G28 and the other transcription factor sequences of the invention would alter a plant's tolerance to resistance or disease, including by enhancing tolerance, as claimed. By this rejection, the Examiner seems to be stating that identifying a transcription factor sequence by expression analysis after fungal pathogen challenge, logically inferring that the transcription factor gene may be used to create transgenic plants with altered fungal disease tolerance, identifying the fungal pathogens to which said plant is tolerant, and then confirming the prophetic component of the claims directed to increasing fungal disease tolerance with rigorous experimental scrutiny (see the Heard declaration, previously submitted), is insufficient to obtain a patent.

E

However, Applicants note that prophetic examples do not make a disclosure non-enabling. Please see: Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984):

> **"[w]ith regard to prophetic examples and enablement, the standard used is not whether a working example exists at the time of filing, but whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art."**

As shown below, the embodiments of the present claims were operative at the time the application was filed. G28 was identified as a transcription factor gene, the G28 polypeptide was identified as a transcription factor that alters tolerance or resistance to pathogens, and the preparation of transgenic plants from genes was routine at the time the instant application was filed. Furthermore, the specification provides examples of transcription factors that were similarly discovered and shown to function by altering disease tolerance (see page 25, lines 3-13 of the specification). Thus, the expenditure of effort required to practice the invention would be no more effort than is normally required in the art. For example, Zhou et al. published a portion of the Pti4 sequence, which has a high degree of similarity to G28 in the conserved domain, and taught that the Pti4 sequence is a transcription factor. Pti4 specifically recognizes and binds to a DNA sequence that is present in the promoter region of a large number of genes encoding PR proteins, and that challenge with a pathogen results in accumulation or EREBP-1 and EREBP-2 (Zhou, p. 3212, column 1, paragraph 2), which have known function (ethylene responsiveness) and "have the highest homology to Pti4" (Zhou, p. 3212, column 1, paragraph 2). After reading the Zhou paper, one of skill in the art would understand that the structurally similar EREBPs, Pti4, Pti5 and Pti6 specifically recognize and bind to a DNA sequence that is present in the promoter region of a large number of genes encoding PR proteins. Since these molecules share structural similarity with G28, and since Pti4 shares a high degree of structural similarity to the conserved domain of G28, as noted by the Examiner (see below), one of skill in the art would conclude that there is a reasonable expectation that G28 would function in a manner similar to Pti4 (as Zhou concluded with respect to the similarities between EREBPs and Pti4 structure and function, as noted above) and other transcription factors that bind to a DNA sequence that is present in the promoter region of PR proteins, i.e., by increasing disease tolerance.

Zhou et al. came to their conclusions in spite of the fact that they did not prepare a transgenic plant to demonstrate that Pti4 confers disease resistance to that plant.

While Zhou does not teach all of the elements of the present claims, one might reasonably conclude that, based on Zhou's work, Applicants need only have:

(a) supplied the G28 sequence (which was done in the priority application in Family _1, on page 17 of the sequence listing, and on page 5, line 10 of the instant specification, and in the instant Sequence Listing);

(b) identified G28 as a transcription factor (e.g., on page 7, line 22, and confirmed by the Examiner in paper 25, page 5, paragraph 2);

(c) determined that G28 had a high degree of similarity to sequences with functions similar to the claimed functions (see, for example, Table 1a, in which G28 is identified as a member of the AP2 family, and the Zhou paper) and

(d) determined that G28 was induced in response to pathogen challenge in order to enable the claimed invention (e.g., on page 7, lines 22-24: "[G28 is] induced when plants are exposed to either biotropic or necrotropic pathogens. These transgenic plants may be more resistant to biotropic or necrotropic pathogens such as a fungus").

all of which Applicants have recognized and taught. In addition to these disclosures, Applicants have disclosed:

(e) how to prepare expression cassettes or vectors (page 12, line 28 through page 13, line 12, and Example III);

(f) how to regulate transcription and processing of the instant transcription factors, including G28 (page 13, line 13 through page 14, line 12);

(g) how to transform plants with the instant transcription factors, including G28 (page 16, line 9 though page 17, line, and Examples IV, page 22, V, page 22, VI, page 23, and VIII, page 25); and

(h) how to identify transformed plants for pathogen resistance or tolerance (Example VII, page 24).

Applicants have gone beyond these steps by teaching how to incorporate these genes, including G28, into expression cassettes or vectors, transform agrobacteria, transform plants, and analyze plants for disease resistance or tolerance, including the use of observational analysis and the detection of induction of resistance associated genes (similar to Zhou) with gene expression microarrays (page 24, lines 15-21).

The instant specification also provides guidance for the manipulation of expression levels of instant transcription factors, including G28, by endogenous means, gene silencing, how to identify homologous sequences, and how the instant transcription factors, including G28, may be modified by

conservative substitutions deletions or additions (page 10, paragraphs 2-3). One wishing to practice the invention would thus find a great wealth of information for the enabling methods in the instant specification. Applicants did show how to identify transcription factors, including G28, using BLAST analysis.

Example VII provides guidance as to how to identify plants transformed with the instant transcription factors that have enhanced disease resistance or tolerance, or induction of resistance-associated genes. Numerous references within the specification and the claims to altered disease tolerance or resistance clearly identify the instant transcription factors, including G28, as sequences that may be used to alter a plant's disease resistance or tolerance. Thus Applicants clearly identified the G28 polynucleotide and polypeptide, SEQ ID NO: 17 and 18, respectively, as having the ability to alter disease tolerance or resistance in a plant (see for example, Claim 1: which identifies "SEQ ID Nos. 2N, where N=1-56, wherein the recombinant polynucleotide alters the plants disease tolerance or resistance"), and correctly predicted that G28 would confer disease tolerance. As is shown in the declaration from Dr. Heard (submitted with the previous response to paper no. 19, the previous Office action,), the function of G28 was analyzed using transgenic plants in which this gene was expressed under the control of the 35S promoter. G28 overexpressing lines were shown to be more tolerant to infections by *Erysiphe orontii*, *Sclerotinia sclerotiorum* or *Botrytis cinerea*, and that mRNA levels of G28 were upregulated at least 3-fold at 24 hours following treatment of native plants with the *Fusarium*.

Thus, the disclosure in the specification, in which it was indicated that the instant transcription factors, including G28, could be used to produce plants that are more tolerant to disease (see, for example, page 7, lines 22-28, page 17, lines 10-17, page 19, line 31 through page 21, line 28, page 24, line 9 through page 25, line 13), was subsequently confirmed by experimentation.

Since prophetic examples do not make the disclosure non-enabling, and since Applicants have provided a wealth of guidance as to the function and methods for using the present transcription factors, including G28, one skilled in the art would be able to practice the invention readily (as (similarly, but not identically) practiced by Zhou et al.). From the high level of skill in the art at the time of filing for identifying transcription factors and their function, the preparation of transgenic plants, and the detail provided in the steps for the preparation and identification of transgenic plants that are disease tolerant, including the experimental successes provided on page 25, lines 3-13 of the specification, one skilled in the art would therefore reasonably conclude that the specification properly enabled the claimed invention at the time of filing, and that Applicants were in possession of the presently claimed invention.

Accordingly, Applicants respectfully request reconsideration and that this part of the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn..

Sections (10-11) of the rejection: 35 U.S.C. § 103(a)

The rejection of the claims under 35 U.S.C. § 103(a) is a new rejection, based on grounds not previously established by the Examiner. The Examiner has not stated that this rejection was necessitated by any action on the part of the Applicants, and, in fact, was not so necessitated for the following reasons.

(1) Claims directed to the conserved domain of G28 (SEQ ID NO: 18) had been previously filed, but had not been rejected under 35 U.S.C. § 103(a). See, for example, claims with the preliminary amendment filed on January 28, 2002, with numerous claims directed to the conserved domain of G28 and other transcription factor genes. This filing was followed by a restriction requirement and rejection under other sections of 35 U.S.C. 35, including § 112, second paragraph, indefiniteness. In response to a previous rejection, Applicants further defined the metes and bounds of the invention by identifying the amino acid coordinates in amended claims, which defining amendment did not substantially change the substance of the claims and thus could not provoke this rejection.

(2) Said conserved domain amino acid coordinates, 145-213, were shown in Table 1a of the Application as filed.

(3) The Examiner has now rejected the claims under 35 U.S.C. § 103(a) when, in fact, the conserved domain of G28 was already present in the claim, and the coordinates could have been identified from Table 1a.

(4) This is the first time the Zhou reference was used as the basis for a rejection, in spite of the fact that all of the same claim elements had been present prior to this rejection.

Accordingly, Applicants request that the finality of this Office action be withdrawn.

The rejection of claims 37, 38, 40-42, 45, 46, 48-50, 53, 54, 56-58, 61, 63-68, and 70-76 under 35 U.S.C. § 103(a) are avoided in part and respectfully traversed in part for the reasons set forth below.

All of the claims except claims 75 and 76 have been amended and are no longer directed to conservative substitutions. Since the prior art and knowledge in the art at the time of filing does not teach or suggest all of the claim elements of the presently-amended claims, the prior art and knowledge in the art cannot be combined to produce the claimed invention.

With regard to claims 75 and 76, the Examiner has failed to set forth a prima facie case for an obviousness rejection. 35 USC 103(a) states a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. The *prima facie* case must satisfy three requirements: 1) the references must teach or suggest all the claim limitations; 2) the prior art combined with general knowledge must include a suggestion or incentive to modify or combine the references; and 3) the modification or combination must have a reasonable chance of success. Furthermore, even when a *prima facie* case has been established, such case may be rebutted by evidence of secondary considerations including unexpected properties or results.

The Examiner has asserted that "(t)he amino acid sequence taught by Zhou in the Pti4 polypeptide comprises residues 145-213 of Applicant's SEQ ID NO: 18, having one or more conservative substitutions, deletions, or insertions. In the event that the Examiner was correct in this statement, the prior reference does not teach tolerance to fungal diseases due to the expression of a transcription factor, including, for example, G28 or G28 with conservative substitutions, deletions, or insertions. The Zhou reference does not teach tolerance to a ***fungal*** disease due to the expression of Pti4; Zhou infers that Pto regulates PR gene expression in tomato via interaction with PR box-binding proteins such as Pti4. Reference is made to PR gene expression (i.e., expression of the targets) activated by biotic stresses including fungal pathogens, but there is no teaching of Pti4 as a transcription factor intermediary. Thus, the references do not teach or suggest all the claim limitations, there is no suggestion to modify or combine the reference with general knowledge to produce the claimed invention, and there is no reasonable chance of success to use or combine the reference with knowledge in the art to create the present invention.

Furthermore, Pti4 does not comprise *the same sequence* as the conserved domain of G28 with one or more conservative substitutions, deletions, or insertions. The conserved domain of G28 and the corresponding Pti4 subsequence, with non-conservative substitutions **emphasized**, are:

G28
GKHYRGVRQRPWGKFAAEIRDPAKNGARVWLGTFETAEDAALAYDRAAFRMRGSRALLNFPLRVNSGEP
Pti4
GRHYRGVRQRPWGKFAAEIRDPAKNGARVWLGTYETAEEAAIAYDKAAYRMRGSKAHLNFPHRIGLNEP

Claims 75 and 76 are specifically directed to "SEQ ID NO: 18, or the same sequence with one or more conservative substitutions, deletions, or insertions". As shown by the above alignment, no matter how many conservative substitutions, deletions, or insertions that are applied to the G28 conserved domain, the instant Pti4 subsequence cannot be created. Thus, the references do not teach or suggest all the claim limitations, there is no suggestion to modify or combine the reference with general knowledge to produce the claimed invention, and there is no reasonable chance of success to use or combine the reference with knowledge in the art to create the present invention.

The instant claims are directed to tolerance to fungal diseases due to the expression of a transcription factor, including, for example, G28 with or without conservative substitutions, deletions, or insertions. The Zhou reference does not teach tolerance to a fungal disease due to the expression of Pti4; Zhou infers that Pto regulates PR gene expression in tomato via interaction with PR box-binding proteins such as Pti4. Reference is made to PR gene expression (i.e., expression of the targets) activated by biotic stresses including fungal pathogens, but there is no teaching of Pti4 as a transcription factor intermediary. The reference describes a challenge with the bacterium *Pseudomonas syringae* pv. *tabaci* in tobacco, followed by expression analysis. Again, the reference does not teach all of the claim elements, and there is no suggestion or motivation in the reference to create the presently claimed invention, and no reasonable expectation that results obtained with *Pseudomonas*, a Gram negative bacterium, would indicate tolerance would be obtained to fungal pathogens.

In addition to the distinct phyla in which the reference pathogen and the claimed pathogens are allocated, Applicants have determined that G28 confers tolerance to multiple fungal pathogens, as noted in the Heard declaration, and to which the claims are directed with the use of the genus " fungal diseases". Furthermore, claims 44, 52, 60, 67, 74, and 76 are specifically directed to multiple pathogens that are identified by name (*Fusarium*, *Erysiphe*, *Sclerotinia* and *Botrytis*). The reference cited by the Examiner does not teach or suggest either tolerance or resistance to *Fusarium*, *Erysiphe*, *Sclerotinia* or *Botrytis*. Transcription factors that are expressed in response to more than one distinct pathogen are relatively rare, and the experimental data showing that G28 confers tolerance to more than one fungal pathogen was a surprising result. The Zhou reference does not teach the expression of Pti4 or disease tolerance induced by more than one pathogen. Thus, the reference does not teach all of the claim elements, there is no suggestion or motivation in the reference to create the presently claimed invention, and there is no reasonable chance of success to use the reference or combine the reference with knowledge in the art to

create the present invention. Furthermore, these experimental results comprise unexpected results or properties, and were predicted in the present specification (see, for example, page 7, lines 22-27).

Accordingly, Applicants respectfully request that this rejection be withdrawn.

Section (12) of the rejection: Provisional Double Patenting Rejection

The Examiner has rejected Claims 17-36 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending applications 09/713,994 and 09/934,455.

As this is a provisional rejection, Applicants will address this rejection when claims of this or the copending application are allowed.

Applicants have previously requested an extension of time of one month in order to respond to the instant Office action. A request for an additional (1) month extension of time is hereby requested, as for which the Commissioner is hereby authorized to charge Deposit Account No. 50-1129. No any other fees or petitions, are believed to be necessary to enter and consider this paper. If, however, any petitions or extensions of time are required or any fees are due in order to enter or consider this paper or enter or consider any paper accompanying this paper, including fees for net addition of claims, or in order to keep this application pending, Applicants hereby request any extensions or petitions necessary and the Commissioner is hereby authorized to charge Deposit Account No. 50-1129 for any fees.

Application No. 09/533,029
Atty Docket No. MBI-0010

Respectfully submitted,

Date: June 3, 2003

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